Synthetic alternative to monoclonal antibodies enter humans for the first time

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New Delhi: In a first ever instance in the world, the US based Inovio Pharmaceuticals in collaboration with The Wistar Institute and the University of Pennsylvania has initiated the first human study of its DNA-encoded monoclonal antibody (dMAb™) technology to prevent Zika virus infection. In addition to demonstrating safety and tolerability, starting at lower and then increasing doses in this Phase 1 dose-escalation study of INO-A002.

When delivered directly into the body, the genetic instructions provided by the designed synthetic dMAbs, instruct the body's cells to become the factory which manufactures the therapeutic antibody products, enabling a major leap in antibody technology.

Dr J Joseph Kim, Inovio's President and CEO, said, "Initiating this first human trial is a milestone for Inovio and a major potential advancement for a potentially breakthrough class of medicines – DNA-encoded monoclonal antibodies – produced directly in the human body via the dMAb technology, pioneered by Inovio and our collaborators. While this trial targets Zika virus infection, we will gain important data from this study towards development of a broad range of our dMAb programs targeting infectious diseases, cancer immunotherapy,

inflammation, as well as therapies for cardiovascular disease. Our goal was to create a new improved approach to monoclonal antibody technology that results in a pipeline of high impact dMAb products, which can be developed with corporate partnerships, external funding and collaborations."

The Wistar Institute was awarded funding via a grant from the Bill & Melinda Gates Foundation to support and advance this innovative research into the clinic. David B. Weiner, Ph.D., executive vice president, director of Wistar's Vaccine & Immunotherapy Center, and the W.W. Smith Charitable Trust Professor in Cancer Research at Wistar, led the research efforts and is working with partners to advance this new generation of DNA-based technologies. This open-label trial is a single center, dose escalation trial will enroll up to 24 healthy volunteers who will receive up to four doses of INO-A002. The trial will be led by Pablo Tebas, M.D., Professor of Medicine at the Hospital of the University of Pennsylvania.

"Through detailed preclinical studies developing this new platform, the team has demonstrated the in vivo production by synthetic DNA technology of dMAbs using the CELLECTRA delivery system," said Weiner. "These antibodies (produced in the body) can display improved kinetics with simple stable formulations providing disease protection in animal challenge models. We are very excited to have contributed to the conception and development of this technology and to participate in this first human trial of a synthetic DNA-encoded monoclonal antibody. This approach represents the potential for major advancement over traditional MAb approaches and may broaden therapeutic strategies and open new patient markets to the benefits of antibody-based therapies for disease prevention or treatment."

Traditional monoclonal antibodies represent the largest segment of pharmaceutical markets today, accounting for more than $100 billion in pharmaceutical sales each year, with treatments spanning cancer, infectious diseases, inflammation and cardiovascular diseases. With its synthetic design and in-patient production, dMAb products represent a disruptive entrant to this important class of pharmaceuticals. Inovio and its collaborators have already received over $60 million in non-dilutive grant funding to advance its dMAb platform in the last few years. There is a significant interest in dMAb's as a disruptive entrant to a highly valuable overall monoclonal antibody market as well as its unique applicability for rapid responses against emerging global infectious disease threats and for addressing critical vaccine limitations.

In just the past few years, Inovio and collaborators have published multiple impactful papers consistently demonstrating potent preclinical data from the dMAb platform, with therapeutic displays spanning protection against deadly infections to eliminating cancers and lowering life-threatening levels of cholesterol. In this regard dMAbs offer unique features for rapid production, deployment and advancement of new MAb-like biologics, with much increased efficiency. In addition, the dMAb's constructed in vivo likely may have additional advantages such as expression profiles, as well as glycosylation, and unlike traditional MAb approaches, there is no reliance on in vivo tissue culture and costly or time-consuming production systems.

Studies such as INO-002 are important to provide the initial data for expanding this valuable platform. In addition, Inovio collaborative studies have recently reported on the development of several dMAb checkpoint inhibitors which in animal studies reproduce faithfully the anti-cancer effects of the biologic molecules. Inovio directly and through their sponsored research has established a significant patent estate in this area.